In the specification:

Replace the paragraph on page 3, lines 4-19 with the amended paragraph below.

Previously, certain genes associated with specific, mental conditions have been disclosed. For example, US 5 783 680 discloses monoxidase genes and proteins associated with abnormal behavior. More specifically, the conditions defined therein are ~~behavioural~~ behavioral disorders, such as impulsive aggression, and include borderline mental retardation and aggressive outbursts, often in response to anger, fear or frustration. Such aggressive ~~behaviour~~ behavior was noted to vary markedly in severity. Other types of impulsive ~~behaviour~~ behavior that occurred in individual cases included arson, ~~attemted~~ attempted rape, and exhibitionism. Thus, as is obvious to one of skill in this field, there are clear differences between the conditions which US 5 783 680 relates to and ~~phsyciatric~~ psychiatric disease, such as schizophrenia. This is evident from the ~~fact,~~ fact that none of the symptoms cited in ~~said~~ US 5 783 680 are found in the DSM-IV diagnostic criteria for schizophrenia or manic depression, nor are the minimal features required for schizophrenia or manic depression present in the family mentioned in US 5 783 680. (For the DSM-IV criteria, see Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition. Copyright 1994 American Psychiatric Association.) Thus, US 5 783 680 does not relate to mutations that can cause ~~psyciatric~~ psychiatric disturbances.

Replace the paragraph on page 8, lines 2-8 with the amended paragraph below.

Actually, after the above-discussed description of mutations in MAOA in patients with impulsive aggression (US 5 783 680), another study (Am J Med Genet 1999 Feb 5;88(1):25-8) was carried out searching for MAOA mutations in patients with similar diagnoses (and also healthy individuals and Parkinson patients who served as control material), without finding any ~~muations~~ mutations. Thus, similarly to the novel mutations according to the present invention, MAOA mutations are very rare causes of certain conditions, which in their case are ~~behavioural~~ behavioral.

Replace the paragraph on page 16, lines 7-18 with the amended paragraph below.

Another aspect of the invention is a method of detecting the presence of a mutation in exon 3 of the Nurr1 gene, which mutation is selected from the group consisting of Met97Val, His103Arg, Tyr121del and Tyr122del, which method comprises obtaining a biological sample from e.g. a human subject or an animal model and analyzing said sample for said mutation. More specfifically, the biological sample is analyzed by isolating DNA for said sample, amplifying said DNA, ~~hybridising~~ and hybridizing said DNA to a labeled oligonucleotide probe that specifically hybridizes to mutant DNA containing a G as the first base of codon no. 97; a G as the second base of codon no. 103; or ~~(how do I say this:)~~ altered TACTAC in codon no. 121 or 122, or to one or more bases adjacent to said mutation, depending on the method used. Methods of detecting mutations in DNA are e.g. reviewed in U. Landgren, GATA 9, pp. 3-8.

Replace the paragraph running from page 19, line 7 through page 20, line 21 with the amended paragraph below.

Figure 3 shows in table 1 the primers used to amplify the PCR fragments 0 to 7. Because no intronic sequences were known when the present study was initiated, primers are located in exons and almost all fragments contain intron sequence. More specifically, fragment no. 0 comprises a part of the second (non-coding) exon, intron 1 (complete) and 2 bases of exon 3; in fragment no. 1, the forward primer is located in the second intron, immediately adjacent to the border to the third exon, and this fragment contains the first 513 bases of exon 3; fragment no. 2 is the second half of exon 3, both primers being located within coding sequence; fragment no. 3 is the rest of exon 3, complete intron 3 and a major part of exon 4; fragment no. 4 comprises exon 4, intron 4 and exon 5; fragment no. 5 comprises exon 5, intron 5 and exon 6; fragment no. 6 comprises exon 6, intron 6 and exon 7; and fragment no. 7 comprises exon 7, intron 7 and exon 8 including 34 bases of 3' untranslated region. Figure 4 provides by table 2 clinical descriptions of the three heterozygous carriers of mutations M1 to M3 according to the invention. In table 2, the following abbreviations are used: MD: Major depression; SAP: Separation Anxiety Disorder; ADHD: Attention Deficit/Hyperactivity Disorder. More specifically, the history of the female heterozygous carrier of M1 is an onset with ~~auditary~~ auditory hallucinations, later displayed delusions of reference, paranoid delusions, verbal auditory hallucinosis, visual and tactile hallucinosis, thought insertion and thought "broadcast", as well as flat and sometimes inappropriate affects. She responded well to antipsychotic treatment but experienced relapses after discontinuation of the antipsychotic medication. She is currently on continuous

antipsychotic medication and has been free from psychotic episodes for several years. Her family history was as follows: The paternal grandmother's sister had been treated at a mental hospital, the cause of illness unknown. The history of the M2 carrier includes a first hospital admission after 5 months of expansive and irritable mood, decreased need for sleep, distractability, and excessive involvement in pleasurable activities. The end of this period also included psychotic symptoms: verbal mood-congruent auditory hallucinations, delusions of reference, grandiose delusions, incoherence, and disorganized ~~behaviour~~ behavior. Treatment was performed with antipsychotic medication and discharge to an outpatient department. Rehospitalization took place a month later due to depressed mood, weight gain, loss of energy, feeling of worthlessness, difficulties to concentrate, and recurrent thought of death. No psychotic symptoms occurred during later manic and depressive episodes. She has currently been treated with lithium for more than four years without relapses. The family history of the M2-carrying patient was as follows: The patient reported no major psychiatric disturbances in the family history. However, the paternal grandfather was said to be a confidence trickster. The history of the M3 carrier includes two episodes of extended depressed mood and anhedonia (ages 6-7 and 10-11). Auditory hallucinations were experienced since the second episode. Hallucinations and delusions occur regularly and are independent of mood state. ~~Intermittent~~ There is an intermittent history of obsessions and compulsions since age of 6. ~~Frequent~~ There have also been frequent episodes of illogical thinking and neologisms and short periods of incoherent speech. The family history of the M3-carrying patient was as follows: The mother reported a few occasional (olfactory, visual) hallucinatory episodes but no further symptoms.

Replace the section on page 23, lines 9-25 with the amended section below.

DNA sequencing

DNA was extracted from whole blood ~~accoring~~ according to standard protocols. The genomic structure of the human Nurr1 gene was deduced from the homologous mouse Nurr1 gene, and primers covering the second exon and the entire coding region were designed (table 1~~, fig 3~~). The numbering of the nucleotides and amino acids employed herein follows the initial publication of the human Nurr1 *(NOT)* mRNA sequence (Mages *et al., supra*). The sequence of the second intron was determined by sequencing of fragment 0, and one additional forward primer was designed located in the second intron (see table 1, ~~figure 3,~~ and figure 1). Polymerase chain reaction (PCR) was carried out using Taq DNA polymerase (SIGMA). 35 cycles were run at 94°C for 40 seconds, 56°C for 45 seconds and 72°C for one minute. After PCR, the samples underwent electrophoresis on 1% low-melting agarose gels and were visualized using UV-translumination after ~~ethidiumbromide~~ ethidium bromide staining. DNA was extracted from gel slices (PCR preps DNA purification kit, SDS) and DNA fragments were sequenced (Thermo Sequenase radiolabeled terminator cycle sequencing kit, Amersham). The reaction products were run on 6% acrylamide sequencing gels (National Diagnostics) and visualized by autoradiography.

Replace the section running from page 24, line 22 through page 25, line 12 with the amended section below.

In-vitro expression assay

Human *NURR1* cDNA sequence was cloned into the expression vector pCMX [Umesono et al., 1991], and expression vectors for the mutants were generated by site-directed mutagenesis (GeneEditor In Vitro Site-Directed Mutagenesis System, Promega). A double-stranded NurRE [Philips et al., 1997] DNA fragment was generated by annealing the primers 5'-AGC TTG TGA TAT TTA CCT CCA AAT GCC AG-3' (SEQ ID NO:1) AND 5'-AGC TCT GGC ATT TGG AGG TAA ATA TCA CA-3' (SEQ ID NO:2). A luciferase reporter plasmid containing three tandem NurRE sites was generated by ligating the annealed fragments upstream of the herpes simplex thymidine kinase promoter fused to the luciferase gene. Human embryonic kidney (HEK)-293 cells were grown in Dulbecco's modified Eagle's medium supplemented with 10% fetal calf serum (FCS). Transfections were performed in 24-well plates by the calcium phosphate method. Briefly, cells were seeded one day prior to transfection. Cells in each well were treated with 100ng of the indicated expression vectors, 100ng of reporter plasmid and 200ng of reference CMX-βgal plasmid containing the β-galactosidase gene and CMX-PL1 as carrier DNA up to 500ng of total DNA. Cells were exposed to calcium phosphate precipitate for 12-16h and washed with PBS and then fresh medium was added. The cells were harvested and lysed after 36h incubation. Extracts were assayed for luciferase and β-galactosidase activity in a microplate luminometer/photometer reader (Lucy-1, Anthos). All luciferase activities were normalized to β-galactosidase activity.

Replace the paragraph on page 25, lines 14-24 with the amended paragraph below.

NURR1 transcriptional activity was measured using human embryonic kidney (HEK)-293 cells monitoring NURR1 homodimer binding to NurRE [Philips et al., 1997]. Each experiment was carried out using two independent clones for the wild-type and mutated vectors, respectively, and activity was measured in at least four separate wells for each clone. A significant reduction (30-40%) of transcriptional activity of mutated NURR1 homodimers was found. This reduction was strikingly similar in all three mutated clones and is consistent with the present finding that the three mutations are clustered in a region of NURR1 which is critically important for transcriptional activation. The ~~avarage~~ average activity and s.e.m. of mutated NURR1 in percent of wildtype activity in all experiments carried out were ΔY122: 0.645 ± 0.024, n=87; H103R: 0.608 ± 0.036, n=87; and M97V: 0.661 ± 0.046, n=54.

Replace Table 1 with the amended table below.

Table 1

Fragment number	Description	Primer sequences
0	Part of the second (noncoding) exon, intron 1 (complete) and 2 bases of exon 3	F-GGAGATTGGACAGGCTGGAC (SEQ ID NO: 3) R-TGCGCCTGAACACAAGGCAT (SEQ ID NO: 4)
1	The forward primer is located in the second intron, immediately adjacent to the border to the third exon. This fragment contains the first 513 bases of exon 3	F-TTATCACCCTGTTTCATTTCC (SEQ ID NO: 5) R-GAGACTGGCGTTTTCCTCT (SEQ ID NO: 6)
2	Second half of exon 3. Both primers are located within coding sequence	F-TGCCGCACTCCGGGTCGGTTTACTACA (SEQ ID NO: 7) R-GCCCTCACAGGTGCGCACGCCGTA (SEQ ID NO: 8)
3	Rest of exon 3, complete intron 3 and major part of exon 4	F-CACGCGTCTCAGCTGCTCGACAC (SEQ ID NO: 9) R-CTTCTTTGACCATCCCAACAGCCA (SEQ ID NO: 10)
4	Exon 4, intron 4 and exon 5	F-CGCACAGTGCAAAAAAATGCAA (SEQ ID NO: 11) R-CCTGGAATAGTCCAGGCTGG (SEQ ID NO: 12)
5	Exon 5, intron 5 and exon 6	F-TGGTTCGCACAGACAGTTTA (SEQ ID NO: 13) R-GCTAATCGAAGGACAAACAG (SEQ ID NO: 14)
6	Exon 6, intron 6 and exon 7	F-TTCCAGGCGAACCCTGACTA (SEQ ID NO: 15) R-ACCATAGCCAGGGCAGCAAT (SEQ ID NO: 16)
7	Exon 7, intron 7 and exon 8 including 34 bases of 3' untranslated region	F-TCCAACCCAGTGGAGGGTAA (SEQ ID NO: 17) R-ATTCCAGTTCCTTTGAAGTGC (SEQ ID NO: 18)

Insert immediately following the claims the Abstract of Disclosure provided herewith on a separate page.

Insert immediately following the Abstract the 5-page Sequence Listing provided herewith on separate pages.